

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 March 2001 (22.03.2001)

PCT

(10) International Publication Number
WO 01/19998 A1

(51) International Patent Classification⁷: C12N 15/31,
15/09, 1/21, A61K 39/108 // (C12N 1/21, C12R 1:19)

Kyonggi-di 463-010 (KR). CHUNG, Soo-il [US/KR];
112-902, Hyundai Apt., Hyoja-chon, Seohyun-dong,
Pundang-ku, Sungnam-si, Kyonggi-do 463-480 (KR).

(21) International Application Number: PCT/KR99/00555

(74) Agent: LEE, Han-Young; Seowon Building, 8th floor,
1675-1, Seocho-dong, Seocho-gu, Seoul 137-070 (KR).

(22) International Filing Date:
15 September 1999 (15.09.1999)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant (for all designated States except US): MOGAM
BIOTECHNOLOGY RESEARCH INSTITUTE
[KR/KR]; 341, Pojung-ri, Koosung-myon, Yongin-si,
Kyonggi-do 449-910 (KR).

(81) Designated States (national): AE, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE,
ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,
VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (for US only): PARK, Eun, Jeong
[KR/KR]; 322-1007, Woosung Apt., Sangrok-maeul,
Jungja-dong, Pundang-ku, Sungnam-si, Kyonggi-do
464-010 (KR). KIM, Jang, Seong [KR/KR]; 902 Ikjoo
Apt., Yeonmoo-dong, Jangan-ku, Suwon, Kyonggi-do
440-240 (KR). CHANG, Jihoon [KR/KR]; 553-517,
Jayang 3-dong, Kwangjin-ku, Seoul 143-193 (KR).
YUM, Jungsun [KR/KR]; 115-502, Chunggu Apt.,
Hansol-maeul, Jungja-dong, Pundang-ku, Sungnam-si,

Published:

— With international search report.

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: NOVEL DETOXIFIED MUTANTS OF *ESCHERICHIA COLI* HEAT-LABILE ENTEROTOXIN

(57) Abstract: The present invention relates to detoxified and immunologically active proteins ("mutant LTs") having mutated amino acid sequences of heat-labile enterotoxin of *E. coli*, DNA sequences encoding the mutant LTs, recombinant expression vectors comprising the DNAs, recombinant microorganisms transformed with the recombinant expression vectors, process for preparing the mutant LTs and pharmaceutical application of the said protein as immunogenic antigens for vaccination and as adjuvants for antibody production. In contrast to wild-type LT, the mutant LTs did not induce any toxic activities. The mutant LTs elicited high and comparable levels of anti-LT antibodies when delivered either intragastrically or intranasally, inducing systemic and local responses in serum and fecal extracts. Thus, they might be useful for the development of a novel diarrheal vaccine in humans and animals. In addition, the antibody production ability using mutant LTs as an adjuvant may be effective for prevention and treatment of various diseases.